

## REMARKS/ARGUMENTS

Claims 1-20 are currently pending in the application. None of the claims have been amended by this response. It is respectfully submitted that the following remarks present no new issues or new matter and place this case in condition for allowance. Reconsideration of the application in view of the following remarks is respectfully requested.

### **I. Rejection of Claims 1-17 under 35 U.S.C. § 103(a)**

Claims 1-17 are rejected under 35 U.S.C. § 103(a) as being obvious over U.S. 4,929,605 to Domet et al. ("Domet") in combination with JP 09315971 to Nakajima et al. ("Nakajima"). The rejection is respectfully traversed.

Domet discloses in examples 1 and 2 (columns 5 and 6), pharmaceutical compositions containing terfenadine, polysorbate 80, calcium carbonate, microcrystalline cellulose, pregelatinized corn starch, starch glycolate sodium, and magnesium stearate. These examples teach compositions containing only terfenadine. Domet does not provide any examples that teach the use of fexofenadine. In addition, the examples of Domet disclose that calcium carbonate is a required component of the Domet composition. The Examiner states "fexofenadine and terfenadine...are quite similar in structure differing "only" by a substituent (i.e. methyl group as opposed to a carboxyl group)." However, there is a significant chemical difference between methyl and carbonyl. Methyl is a non-reactive and non-polar moiety, while carbonyl is highly polar and very reactive. The structural difference results in a dramatic difference in the pharmacological properties of the molecules. Terfenadine is no longer marketed having been discontinued because of potentially lethal cardiac side effects, while fexofenadine is presently being commercially marketed. Thus, fexofenadine is not equivalent to terfenadine.

The Examiner states "Nakajima et al disclose that their terfenadine-containing tablet preparation which is prepared by combining terfenadine with specific components in specific proportions, readily disintegrate, and the terfenadine contained therein is released favorably (page 3, [001-003]." It is noted that in paragraph [0008], lines 10-12, Nakajima further adds "it has been found that a particularly favorable combination is low-substituted hydroxylpropyl cellulose and precipitated calcium carbonate." One of ordinary skill in the art would conclude from these statements that calcium carbonate must be used to achieve a tablet that readily disintegrates and results in a favorable release of terfenadine.

Further, the motivation or suggestion to combine references in the manner suggested by the Examiner must come from the applied references. There is no disclosure, direction, or

motivation in either Domet or Nakajima to suggest the combination asserted by the Examiner. There is no motivation in the art for one skilled to combine Domet with Nakajima as suggested by the Examiner. Domet states in column 1, lines 30-33 "[a] novel pharmaceutical composition is now provided which allows efficient and immediate absorption bioavailability of these compounds after oral administration." One skilled in the art would conclude that Domet has provided a successful, working formulation, and there would be no motivation to combine any part of Nakajima's composition to Domet's composition.

Assuming arguendo, even if motivation to combine the references in the manner suggested by the Examiner did exist in the applied references, the resultant combination still would not disclose Applicants' claimed invention. One skilled in the art would conclude from the teachings of both Domet and Nakajima that calcium carbonate is an essential component that must be included in order to achieve a bioavailable composition. Applicants' invention as claimed does not include calcium carbonate, and through the use of "consisting essentially of" language in Claim 1, applicants have excluded the use calcium carbonate that would materially affect the basic and novel characteristics applicants' invention as claimed. Thus, the Examiner has not established a prima facie case for obviousness under 35 U.S.C. § 103.

## **II. Rejection of Claims 18-20 under 35 U.S.C. § 103(a)**

Claims 18-20 are rejected under 35 U.S.C. § 103(a) as obvious over in Nakajima combination with Domet.


The Examiner states it would have been obvious to one skilled in the art to have used the method of Nakajima to prepare a pharmaceutical composition comprising fexofenadine, lactose, and low-substituted hydroxypropyl cellulose.

Nakajima discloses a pharmaceutical composition prepared by (a) wet granulating terfenadine, lactose, corn starch, low-substituted hydroxypropyl cellulose, precipitated calcium carbonate, hydroxypropyl cellulose; (b) drying the granules; (c) sifting the granules; and (e) mixing with magnesium stearate. As discussed previously, calcium carbonate is essential to both Nakajima's and Domet's composition. Through the use of "consisting essentially of" language in Claims 18 and 19, applicants have excluded the use of ingredients such as calcium carbonate that would materially affect the basic and novel characteristics applicants' invention as claimed.

In view of the above, it is respectfully submitted that all of the claims are in condition for allowance, and a Notice of Allowance is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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